

Mary

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65586

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: P. Spivack Examiner #: 70400 Date: 4/29/02
Art Unit: 1614 Phone Number 30 84703 Serial Number: 09/978/32
Mail Box and Bldg/Room Location: 2D05 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. m.e.j.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Steven Curtis Zicker

Inventors (please provide full names): Karen J. Wedekind

Earliest Priority Filing Date: 10/31/2000

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search:

new? degenerate?
neurodegenerative disorder
dementia cognit?

methods for decreasing mental deterioration or
increasing mental capacity
comprising administering an antioxidant (such as
lipoic acid or vitamin C [ascorbic acid] or vitamin E
in a cat (feline) or
a dog (canine) diet. or l-carnitine)

Mary Hale - Supervisor, Info. Branch
STIC - Biotech/Chem. Library
CM-1 Room E01
703-308-4258

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	Type of Search	Vendors and cost where applicable
Searcher: <u>Mary</u>	NA Sequence (#)	STN <u>12476 (36-42)</u>
Searcher Phone #:	AA Sequence (#)	Dialog
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Date Searcher Picked Up: <u>5/2</u>	Bibliographic <input checked="" type="checkbox"/>	Dr.Link
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Online Time:	Other	Other (specify)

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COST IN U.S. DOLLARS

SINCE FILE
ENTRY
12.26

TOTAL
SESSION
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Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES

Searched by: Mary Hale 308-4258 CM-1 12D16

for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

```
=> s (lipoic acid or vitamin c or ascorbic acid or vitamin e or "l-carnitine")/cn
      2 LIPOIC ACID/CN
      1 VITAMIN C/CN
      2 ASCORBIC ACID/CN
      1 VITAMIN E/CN
      1 "L-CARNITINE"/CN
L1      6 (LIPOIC ACID OR VITAMIN C OR ASCORBIC ACID OR VITAMIN E OR "L-CARNITINE")/CN
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	ENTRY	SESSION
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FILE 'WPIDS' ENTERED AT 15:30:56 ON 02 MAY 2002
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=> s (lipoic acid or vitamin c or ascorbic acid or vitamin e or "l-carnitine" or
l1)
L2      50638 FILE MEDLINE
L3      111575 FILE CAPLUS
L4      54288 FILE BIOSIS
L5      48534 FILE EMBASE
L6      7201 FILE JICST-EPLUS
L7      13100 FILE WPIDS
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TOTAL FOR ALL FILES

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L8      285336 (LIPOIC ACID OR VITAMIN C OR ASCORBIC ACID OR VITAMIN E OR "L-CARNITINE" OR L1)
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=> s l8 and ((mental or neur?)(5a)(degenerat? or deteriorat? or capacit?) or
neurodegenerat? or dementia)
L9      389 FILE MEDLINE
L10     319 FILE CAPLUS
L11     329 FILE BIOSIS
L12     628 FILE EMBASE
L13     43 FILE JICST-EPLUS
L14     102 FILE WPIDS
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Searched by: Mary Hale 308-4258 CM-1 12D16

TOTAL FOR ALL FILES

L15 1810 L8 AND ((MENTAL OR NEUR?) (5A) (DEGENERAT? OR DETERIORAT? OR CAPACIT?) OR NEURODEGENERAT? OR DEMENTIA)

=> s (antioxida? or anti oxid?) and ((mental? or neur?) (5a) (degenerat? or deteriorat? or capacit?) or neurodegenerat? or dementia)

L16 799 FILE MEDLINE

L17 815 FILE CAPLUS

L18 796 FILE BIOSIS

L19 828 FILE EMBASE

L20 51 FILE JICST-EPLUS

L21 173 FILE WPIDS

TOTAL FOR ALL FILES

L22 3462 (ANTIOXIDA? OR ANTI OXID?) AND ((MENTAL? OR NEUR?) (5A) (DEGENERAT? OR DETERIORAT? OR CAPACIT?) OR NEURODEGENERAT? OR DEMENTIA)

=> s (l15 or l22) and (diet? or nutrit? or nutrien?) and (cat or feline or kitten or dog or canine or puppy)

L23 2 FILE MEDLINE

L24 1 FILE CAPLUS

L25 4 FILE BIOSIS

L26 2 FILE EMBASE

L27 0 FILE JICST-EPLUS

L28 2 FILE WPIDS

TOTAL FOR ALL FILES

L29 11 (L15 OR L22) AND (DIET? OR NUTRIT? OR NUTRIEN?) AND (CAT OR FELINE OR KITTEN OR DOG OR CANINE OR PUPPY)

=> dup rem l29

PROCESSING COMPLETED FOR L29

L30 10 DUP REM L29 (1 DUPLICATE REMOVED)

=> d cbib abs 1-10;s wedekind, k?/au,in

L30 ANSWER 1 OF 10 WPIDS (C) 2002 THOMSON DERWENT

AN 2002-105552 [14] WPIDS

CR 1998-557054 [47]; 2001-373633 [35]

AB US2001041741 A UPAB: 20020301

NOVELTY - **Nutritional** supplement comprises **L-carnitine**, Coenzyme Q10 (Ubiquinone) or their functional analogs and taurine or its precursor.

ACTIVITY - Cardiant; Anti-HIV; Cytostatic; Immunomodulator; Antibacterial; Immunosuppressive; Nephrotropic; Respiratory; Immunostimulant; Muscular.

MECHANISM OF ACTION - None given.

USE - For treating a disease, disorder or abnormal physical state consisting of heart disease and functional **deterioration** associated with ageing or increasing **neuromuscular** or athletic performance in mammals such as **dogs, cats** and preferably humans (claimed). Also useful in treatment of chronic degenerative disease, immune diseases such as AIDS, chronic multisystem disease, chronic lung or renal disease, chronic fatigue syndrome, patients on immunosuppressive drug post-transplantation, cancer patients on doxorubicin or related drugs, wasting or cachexia from cancer or sepsis.

ADVANTAGE - The composition potentiates the action of each component on cell function and energetics. The composition provides a more reliable and effective treatment to various diseases. The composition also corrects abnormalities in myocardial energetics, intracellular calcium and oxidative stress. The composition maintains and restores mitochondrial

function and prevents cardiac failure and aids recovery from cardiac disease.

Dwg.0/6

L30 ANSWER 2 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2001:472167 Document No.: PREV200100472167. The effects of experience and **antioxidants** on size discrimination learning in the **dog**. Rick, J. T. (1); Ikeda-Douglas, C. J.; Murphey, H.; Muggenberg, B.; Zicker, S.; Milgram, N. W. (1). (1) Dept. of Psychology, University of Toronto, Toronto, ON USA. Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 280. print. Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001 ISSN: 0190-5295. Language: English. Summary Language: English.

AB Free radicals such as O⁻ are byproducts of cellular metabolism and are thought to play a role in **neural degeneration** and age-related cognitive impairment. Using a variety of visual tasks, we have examined age-related deficits in a **canine** model of cognition. Previously, we found cognitive impairments in old **dogs** to be dependent on task difficulty and previous experience (Milgram et al., 1994, Behav. Neurosci. 108:57-68). In the present experiment, we studied the effects of environmental enrichment and an **antioxidant-rich diet** on the learning ability of aged beagles using a size discrimination reversal task (2 between- and 1 within-subjects factors). Using blocks differing only in size, animals were taught to approach one block over the other. On reaching the performance criterion, the reward contingency was reversed and the **dogs** were required to approach the previously unrewarded block. We found that there was a significant effect of **nutrition**, with animals on the enriched **diet** performing better than those on the control **diet**. The **dogs** in the control environment committed significantly more errors on the reversal, suggesting that enrichment improves an animal's ability to deal with changes in environmental contingencies.

L30 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2001:472166 Document No.: PREV200100472166. The effects of **diet** and age on the performance of the landmark discrimination learning task. Estrada, J. (1); Ikeda-Douglas, C.; Milgram, N. W.; Zicker, S.. (1) Inst Med Sci, University of Toronto, Toronto, ON Canada. Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 279. print. Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001 ISSN: 0190-5295. Language: English. Summary Language: English.

AB Free radicals, which are byproducts of oxidative reactions, are an essential factor in the **degenerative neural** changes that accompany aging. We fed 19 old beagle **dogs** (10-14 years of age) a **diet** consisting of a broad spectrum of **antioxidants** and tested the effects on series of landmark discrimination problems (Land-0, 1 and 2). The task required the animals to respond selectively to the object closest to an external landmark. This task is particularly useful in identifying age-dependent cognitive impairment. The **dogs** were divided into 2 groups receiving control or an **antioxidant-enriched diet**. Animals on enriched **diet** learned the landmark task (Land-1) more rapidly than **dogs** on the control **diet**. These results show that performance in allocentric task can be improved by the administration of an **antioxidant enriched diet**.

L30 ANSWER 4 OF 10 MEDLINE

DUPLICATE 1

2001541737 Document Number: 21473529. PubMed ID: 11588988. Assessment of **dietary** therapies in a **canine** model of Batten disease.

Siakotos A N; Hutchins G D; Farlow M R; Katz M L. (Department of Pathology, Indiana University School of Medicine, 635 Barnhill Drive,

Indianapolis, IN 46202, USA.. asiakoto@iupui.edu) . EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY, (2001) 5 Suppl A 151-6. Journal code: DGS; 9715169. ISSN: 1090-3798. Pub. country: England: United Kingdom. Language: English.

AB The neuronal ceroid lipofuscinoses (NCLs) are inherited **neurodegenerative** diseases that occur in a number of animal species, including **dogs**. A study was conducted to determine whether the resupply of **nutrients** lost in NCL English Setter **dogs** would modify the course of the disease. Carnitine and polyunsaturated fatty acids have been reported to be reduced in NCL English Setters. Therefore, the normal laboratory **diets** of NCL **dogs** were supplemented with carnitine, fish oil and corn oil and the disease progression was compared with that of an untreated litter mate. The following specific prognostic indicators of NCL were monitored: cognitive function, brain atrophy, brain glucose metabolism and lifespan. Carnitine, with or without lipid supplements, dramatically delayed the progression of cognitive decline in NCL **dogs**. When fish oil and corn oil only were supplied, brain atrophy was reduced. A combination of all three supplements preserved cognitive function and increased lifespan by 10%. However, brain glucose hypometabolism and cerebral atrophy were not reduced. The results in this study indicated that the effectiveness of therapeutic interventions can be assessed by non-invasive methods at a relatively early stage of the disease process. Our study suggests that **dietary** supplementation with carnitine is a promising new approach for delaying or preventing the cognitive decline in **dogs**, and perhaps, with human NCL patients.

L30 ANSWER 5 OF 10 WPIDS (C) 2002 THOMSON DERWENT

AN 2000-514772 [46] WPIDS

AB WO 200044375 A UPAB: 20000921

NOVELTY - Method for increasing the plasma **vitamin E** level in a **cat** or **dog** comprises administration of sufficient **vitamin E**, optionally with also **vitamin C**, taurine, and/or a carotenoid; and a **dog** or **cat** foodstuff which delivers a sufficient concentration of ingredients to increase the **antioxidant** status of the animal.

DETAILED DESCRIPTION - Method for increasing the plasma **vitamin E** level in a **cat** or **dog**, by administration of sufficient **vitamin E**, optionally also with addition of **vitamin C** and/or taurine and/or a carotenoid, either simultaneously, separately, or sequentially, is new.

INDEPENDENT CLAIMS are included for:

(1) a **dog** or **cat** foodstuff which delivers a sufficient concentration of ingredients to increase the **antioxidant** status of the animal;

(2) use of **vitamin E** in the manufacture of a clinical **diet** for the prevention or treatment of any disorder which has a component of oxidative stress (sic; the previous limitation to **dogs** and **cats** is omitted); and

(3) a **dog** or **cat** food containing **vitamin C** at a 15 mg/400 kcal or above.

ACTIVITY - **Antioxidant**; Cytostatic; Cardiant; Antiarteriosclerotic; Antiarthritic; Ophthalmological; Antiinflammatory; Nephrotropic; Neuroprotective; Immunostimulant.

MECHANISM OF ACTION - None given.

USE - The **vitamin E** and/or **C**, optionally including also taurine and/or carotenoid, is of use in conditions resulting from oxidative stress, resulting in a healthier animal. These conditions include cancer, aging, heart disease, atherosclerosis, arthritis, cataracts, inflammatory bowel or renal disease, renal failure, **neurodegenerative** disease, or compromised immunity. The composition is also of value in treating or assisting the animal in

response to an immunological challenge, e.g. vaccination, optimizing and/or boosting the desired effect.

ADVANTAGE - **Vitamins E** and **C** are synergistic and complement each other, one being lipid-soluble and the other water-soluble.
Dwg.0/9

L30 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:76899 Document No.: PREV200100076899. Landmark discrimination learning in aged **dogs** is improved by treatment with an **antioxidant** enriched **diet**. Milgram, N. W. (1); Estrada, J.; Ikeda-Douglas, C.; Castillo, J.; Head, E.; Cotman, C. W.; Murphey, H.; Holowachuk, D.; Muggenburg, B.; Zicker, S.. (1) Univ Toronto, Toronto, ON Canada. Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-193.9. print. Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience. ISSN: 0190-5295. Language: English. Summary Language: English.

AB Reactive oxygen species, which are byproducts of cellular metabolism, are potentially critically important contributors to **degenerative neural** changes that accompany aging. We fed a **canine diet** consisting of a broad spectrum of **antioxidants** and tested the effects on age-dependent cognitive deterioration in beagle **dogs**. Young and aged beagle **dogs** were each divided into groups receiving either control or **antioxidant**-enriched **diets**. The **dogs** were placed on the **diet** for either 0 or 5 weeks, and were then tested on a series of discrimination problems, all of which required the animals to respond selectively to the object closest to an external landmark. The aged animals on the enriched **diet** learned all of the tasks more rapidly than did the aged animals on the control **diet**. More consistent improvement was seen initially in the animals given 5 weeks of **diet** before testing. The young animals, by contrast, showed no effect of **diet**. These results both further support a free radical model of age-dependent **neurodegeneration** and indicate that short-term administration of **antioxidants** can partially reverse the deleterious effects of aging on cognition.

L30 ANSWER 7 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:8982 Document No.: PREV200000008982. Multiple **antioxidants** in the prevention and treatment of Parkinson's disease. Prasad, Kedar N. (1); Cole, William C.; Kumar, Bipin. (1) UCHSC, 4200 E. 9th Ave., Denver, CO, 80262 USA. Journal of the American College of Nutrition, (Oct., 1999) Vol. 18, No. 5, pp. 413-423. ISSN: 0731-5724. Language: English. Summary Language: English.

AB Parkinson's disease (PD) is one of the major progressive neurological disorders for which no preventative or long-term effective treatment strategies are available. Epidemiologic studies have failed to identify specific environmental, **dietary** or lifestyle risk factors for PD except for toxic exposure to manganese, meperidine (Demerol(R)), the "designer drug" version of which often contains a toxic byproduct of the synthesis, 1-methyl-4-phenyl 1,2,3,6 tetrahydropyridine (MPTP)), and some herbicides and pesticides. The search for genetic risk factors such as mutation, overexpression or underexpression of nuclear genes in DA neurons in idiopathic PD has not been successful as yet. Polymorphism in certain genes appears to be a risk factor, but there is no direct evidence for the causal relationship between polymorphism and increased risk of PD. In familial PD, mutation in the alpha-synuclein gene is associated with the disease, but a direct role of this gene in **degeneration** of DA **neurons** remains to be established. Although mutations in the Parkin gene has been associated with autosomal recessive juvenile Parkinson's disease, the role of this gene mutation in causing

degeneration of DA neurons has not been defined. We have reported that in hereditary PD, a mutation in the alpha-synuclein gene may increase the sensitivity of DA neurons to neurotoxins. We hypothesize that, in idiopathic PD, epigenetic (mitochondria, membranes, protein modifications) rather than genetic events are primary targets which, when impaired, initiate **degeneration** in DA neurons, eventually leading to cell death. Although the nature of **neurotoxins** that cause **degeneration** in DA neurons in PD is not well understood, oxidative stress is one of the intermediary risk factors that could initiate and/or promote **degeneration** of DA neurons. Therefore, supplementation with **antioxidants** may prevent or reduce the rate of progression of this disease. Supplementation with multiple **antioxidants** at appropriate doses is essential because various types of free radicals are produced, **antioxidants** vary in their ability to quench different free radicals and cellular environments vary with respect to their lipid and aqueous phases. L-dihydroxyphenylalanine (L-dopa) is one of the agents used in the treatment of PD. Since L-dopa is known to produce free radicals during its normal metabolism, the combination of L-dopa with high levels of multiple **antioxidants** may improve the efficacy of L-dopa therapy.

L30 ANSWER 8 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

93311433 EMBASE Document No.: 1993311433. Neuroprotective actions of glucocorticoid and nonglucocorticoid steroids in acute neuronal injury. Hall E.D.. Central Nervous System Diseases Res., Upjohn Company, Kalamazoo, MI 49001, United States. Cellular and Molecular Neurobiology 13/4 (415-432) 1993.

ISSN: 0272-4340. CODEN: CMNEDI. Pub. Country: United States. Language: English. Summary Language: English.

AB 1. The glucocorticoid steroid methylprednisolone (MP) has been shown to enhance chronic recovery after human spinal cord injury when administered in a 24-hr high-dose regimen beginning within 8 hr. The doses of MP that affect this improved recovery have been demonstrated to inhibit posttraumatic spinal cord lipid peroxidation (LP), which has been postulated to be a key event in the secondary injury-induced degenerative cascade. 2. The molecular mechanism of action of the steroid appears to involve intercalation into the cell membrane and blockade of the propagation of peroxidative reactions. At a physiological level, the inhibition of injury-induced LP has been found to result in an attenuation of progressive posttraumatic ischemia and energy failure together with an augmented reversal of intracellular calcium accumulation. However, MP also acts directly to retard secondary **neuronal degeneration** as observed in studies showing the steroid's ability to slow the anterograde degeneration of experimentally injured **cat** soleus motor nerves. 3. The duplication of this effect by the nonsteroidal lipid **antioxidant** .alpha.- tocopherol supports the notion that is indeed a manifestation of the inhibition of posttraumatic LP. Moreover, the efficacy of MP in limiting lipid peroxidation and secondary spinal cord or motor nerve degeneration has also been duplicated by a nonglucocorticoid 21-aminosteroid tirilazad mesylate (U-74006F), which suggests the independence of the **antioxidant** and glucocorticoid effects of MP.

L30 ANSWER 9 OF 10 MEDLINE

90133985 Document Number: 90133985. PubMed ID: 2614850. Mechanisms of **neuronal degeneration** secondary to central nervous system trauma or ischemia. Hall E D; Yonkers P A. JOURNAL OF NEUROTRAUMA, (1989 Winter) 6 (4) 227-8. Journal code: J82; 8811626. ISSN: 0897-7151. Pub. country: United States. Language: English.

L30 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 12D16

1970:10426 Document No. 72:10426 **Vitamin E** deficiency
and fat stress in the **dog**. Hayes, K. C.; Nielsen, S. W.;
Rousseau, J. E., Jr. (Univ. of Connecticut, Storrs, Conn., USA). J.
Nutr., 99(2), 196-209 (English) 1969. CODEN: JONUAI.

AB Thirty-two male beagle **puppies** were fed **vitamin**
E-deficient **diets** with 4 levels (1, 5, 10, and 15%) of
safflower oil with or without a **vitamin E** supplement
for a 15-week period. The unsupplemented **dogs** developed a
vitamin E deficiency which was correlated with increased
dialuric acid hemolysis of red cells and decreased plasma tocopherol
values. Both Hb and packed cell vol. were depressed by increasing fat
consumption, unrelated to tocopherol supplementation and attributed to in
vivo red cell disruption. Creatine phosphokinase values were elevated in
tocopherol-deficient **dogs** and were correlated with fat
consumption. Terminal plasma vitamin A concns. were lower in **dogs**
receiving <1% supplementary fat. At necropsy, browning of the intestinal
muscularis in the tocopherol-deficient **dogs** was related to the
consumption of polyunsatd. fats (PUFA). Microscopically, lipofuscin was
seen in smooth muscle of gut, urinary bladder, and small arterioles.
Neuroaxonal dystrophy and myo-**degeneration** were also
found in the **vitamin E**-deficient **dogs**. The
requirement for tocopherol was directly related to PUFA consumption,
apparently assocd. with the metabolism of the fat and not with an
antioxidant role of the vitamin.

'IN' IS NOT A VALID FIELD CODE

L31 18 FILE MEDLINE
L32 20 FILE CAPLUS
L33 38 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L34 7 FILE EMBASE
L35 0 FILE JICST-EPLUS
L36 3 FILE WPIDS

TOTAL FOR ALL FILES

L37 86 WEDEKIND, K?/AU,IN

=> s zicker, s?/au,in

'IN' IS NOT A VALID FIELD CODE
L38 15 FILE MEDLINE
L39 9 FILE CAPLUS
L40 20 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L41 4 FILE EMBASE
L42 0 FILE JICST-EPLUS
L43 1 FILE WPIDS

TOTAL FOR ALL FILES

L44 49 ZICKER, S?/AU,IN

=> s 137 and 144

L45 0 FILE MEDLINE
L46 0 FILE CAPLUS
L47 0 FILE BIOSIS
L48 0 FILE EMBASE
L49 0 FILE JICST-EPLUS
L50 0 FILE WPIDS

TOTAL FOR ALL FILES

L51 0 L37 AND L44

Searched by: Mary Hale 308-4258 CM-1 12D16

```
=> s (l37 or l44)
L52      33 FILE MEDLINE
L53      29 FILE CAPLUS
L54      58 FILE BIOSIS
L55      11 FILE EMBASE
L56      0 FILE JICST-EPLUS
L57      4 FILE WPIDS
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TOTAL FOR ALL FILES
L58      135 (L37 OR L44)
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```
=> s l58 and ((mental? or neur?)(5a)(degenerat? or deteriorat? or capacit?) or
neurodegenerat? or neuro degenerat? or dementia? or mental?)
```

```
L59      0 FILE MEDLINE
L60      0 FILE CAPLUS
L61      3 FILE BIOSIS
L62      0 FILE EMBASE
L63      0 FILE JICST-EPLUS
L64      0 FILE WPIDS
```

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TOTAL FOR ALL FILES
L65      3 L58 AND ((MENTAL? OR NEUR?)(5A)(DEGENERAT? OR DETERIORAT? OR
CAPACIT?) OR NEURODEGENERAT? OR NEURO DEGENERAT? OR DEMENTIA?
OR MENTAL?)
```

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=> d 1-3 cbib abs
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L65. ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:472167 Document No.: PREV200100472167. The effects of experience and
antioxidants on size discrimination learning in the dog. Rick, J. T. (1);
Ikeda-Douglas, C. J.; Murphey, H.; Muggenberg, B.; Zicker, S.;
Milgram, N. W. (1). (1) Dept. of Psychology, University of Toronto,
Toronto, ON USA. Society for Neuroscience Abstracts, (2001) Vol. 27, No.
1, pp. 280. print. Meeting Info.: 31st Annual Meeting of the Society for
Neuroscience San Diego, California, USA November 10-15, 2001 ISSN:
0190-5295. Language: English. Summary Language: English.

AB Free radicals such as O- are byproducts of cellular metabolism and are
thought to play a role in **neural degeneration** and
age-related cognitive impairment. Using a variety of visual tasks, we have
examined age-related deficits in a canine model of cognition. Previously,
we found cognitive impairments in old dogs to be dependent on task
difficulty and previous experience (Milgram et al., 1994, Behav. Neurosci.
108:57-68). In the present experiment, we studied the effects of
environmental enrichment and an antioxidant-rich diet on the learning
ability of aged beagles using a size discrimination reversal task (2
between- and 1 within-subjects factors). Using blocks differing only in
size, animals were taught to approach one block over the other. On
reaching the performance criterion, the reward contingency was reversed
and the dogs were required to approach the previously unrewarded block. We
found that there was a significant effect of nutrition, with animals on
the enriched diet performing better than those on the control diet. The
dogs in the control environment committed significantly more errors on the
reversal, suggesting that enrichment improves an animal's ability to deal
with changes in environmental contingencies.

L65 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:472166 Document No.: PREV200100472166. The effects of diet and age on the
performance of the landmark discrimination learning task. Estrada, J. (1);
Ikeda-Douglas, C.; Milgram, N. W.; Zicker, S.. (1) Inst Med Sci,
University of Toronto, Toronto, ON Canada. Society for Neuroscience
Abstracts, (2001) Vol. 27, No. 1, pp. 279. print. Meeting Info.: 31st

Annual Meeting of the Society for Neuroscience San Diego, California, USA
November 10-15, 2001 ISSN: 0190-5295. Language: English. Summary Language:
English.

AB Free radicals, which are byproducts of oxidative reactions, are an essential factor in the **degenerative neural** changes that accompany aging. We fed 19 old beagle dogs (10-14 years of age) a diet consisting of a broad spectrum of antioxidants and tested the effects on series of landmark discrimination problems (Land-0, 1 and 2). The task required the animals to respond selectively to the object closest to an external landmark. This task is particularly useful in identifying age-dependent cognitive impairment. The dogs were divided into 2 groups receiving control or an antioxidant-enriched diet. Animals on enriched diet learned the landmark task (Land-1) more rapidly than dogs on the control diet. These results show that performance in allocentric task can be improved by the administration of an antioxidant enriched diet.

L65 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2001:76899 Document No.: PREV200100076899. Landmark discrimination learning in aged dogs is improved by treatment with an antioxidant enriched diet. Milgram, N. W. (1); Estrada, J.; Ikeda-Douglas, C.; Castillo, J.; Head, E.; Cotman, C. W.; Murphey, H.; Holowachuk, D.; Muggenburg, B.; Zicker, S.. (1) Univ Toronto, Toronto, ON Canada. Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-193.9. print. Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience. ISSN: 0190-5295. Language: English. Summary Language: English.

AB Reactive oxygen species, which are byproducts of cellular metabolism, are potentially critically important contributors to **degenerative neural** changes that accompany aging. We fed a canine diet consisting of a broad spectrum of antioxidants and tested the effects on age-dependent cognitive deterioration in beagle dogs. Young and aged beagle dogs were each divided into groups receiving either control or antioxidant-enriched diets. The dogs were placed on the diet for either 0 or 5 weeks, and were then tested on a series of discrimination problems, all of which required the animals to respond selectively to the object closest to an external landmark. The aged animals on the enriched diet learned all of the tasks more rapidly than did the aged animals on the control diet. More consistent improvement was seen initially in the animals given 5 weeks of diet before testing. The young animals, by contrast, showed no effect of diet. These results both further support a free radical model of age-dependent **neurodegeneration** and indicate that short-term administration of antioxidants can partially reverse the deleterious effects of aging on cognition.

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ENTRY	SESSION
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